S. 1477 PROVISIONS THAT UNDERCUT SAFETY & EFFICACY

Shortened Review Times Without Additional Resources. Without providing new resources, S.1477 would require FDA to meet extremely short deadlines (e.g., 4-6 months for drugs). As a result, reviewers may have to approve drugs or devices based on less information, with fewer analyses and much greater uncertainty about the products' safety and efficacy. The agency also may have to strip away all work other than product approval reviews. This will adversely impact other programs (e.g., blood safety, product tampering, mammography).

Statutory Hammers. Pursuant to section 402, if FDA does not, within 60 days of receiving a request, provide binding written classification of a product, the classification designated by the requestor shall be final. Section 404 requires FDA to contract for outside review if in any fiscal year it fails to meet the statutory time frame for 95% of the applications in a particular category. Section 404 deems a product approved when the third party determines that it should be approved.

Sound medical practice. Section 407 would establish a procedure for recognizing new uses of existing drugs and devices based on sound medical practice (i.e., a use that has existed for five years, is "common" among experienced clinicians, and is reasonably based on experience and other confirmatory evidence). This provision would completely bypass the approval process.

The Drug Approval Standard. Section 602 states that substantial evidence may consist of data from one well-controlled clinical investigation and confirmatory evidence. This may lower the effectiveness requirement from two well-controlled studies to, at most, one. Although FDA often accepts data from one well controlled trial, this should not be the standard. Section 410 provides that for efficacy supplements, the data may consist entirely of information published in medical literature if the proposed condition of use relates to treatment of a life-threatening disease. Although FDA has, on occasion, relied on studies published in journal articles to approve an efficacy supplement, this is not and should not be the general rule.

Limits FDA's Review of Safety and Efficacy. Section 304 provides that a protocol shall be designed so that the fewest number of patients and procedures necessary to obtain data necessary for the approval of a product are required. The result will be to limit what FDA can learn about the effect of a product in certain patient populations, such as the elderly or women. Section 408 appears to prohibit FDA from including, in the labeling, indications for which a product is known not to be effective.

Off-label promotion. Section 407 would allow companies to distribute journal articles and other types of information (such as textbook chapters, continuing medical education materials, etc.) to promote unapproved uses. This provision allows manufacturers to promote uses that have not been proven safe and effective. Moreover, it reduces the incentive for companies to do the scientific research and have the new uses reviewed by FDA (in fact, there would be a disincentive because FDA might determine that the new use is not supported by the evidence).

Substantial equivalence determinations. Section 702(c) would recognize any use "included within a general use for a predicate device" as an approved use for 510(k) devices. This would allow a device originally marketed for one clinical indication to later be marketed for other indications, with only the submission of an abbreviated application (510(k)) that would not document the product's effectiveness for the new indication. The provision's effect is to virtually eliminate approval of devices for specific uses.

Device modifications. Section 702(d) would eliminate FDA's role in assuring that modifications made to a product do not adversely affect its safety and effectiveness. Under the bill, unless the manufacturer's own data shows the safety and effectiveness were to diminish, FDA could not require data on the modified product.

The Device Approval Standard. Section 703 would require the agency to accept retrospective or historical clinical data as a control or for determining the effectiveness of a device if sufficient valid data are available and the effects of the device are clearly defined and well understood. The provision indicates a preference for a lower quality of evidence.

Automatic exemption of all class I devices. Section 702(a) exempts all class I devices from premarket notification. FDA has already exempted 572 class I devices. Many of the 216 devices that FDA has not exempted, were not exempted for public health reasons.

KASSEBAUM BILL – SUPPORTABLE CONCEPTS

The following concepts, which are included in S.1477, are supportable. Some of the provisions implementing the concepts, however, require technical or other changes.

Performance Standards. Section 103 requires FDA to develop performance standards for activities ranging from product review to letters and telephone calls. The concept of FDA accountability is supportable, but it should be accomplished in a manner that does not micromanage the agency.

Interagency Collaboration. Section 104 requires FDA to implement programs and policies to foster collaboration between FDA, NIH, and other science-based agencies. The policies underlying this provision (to enhance scientific expertise) are beneficial.

Policy Statements. Section 106 requires FDA to develop a procedure governing the development and use of policy statements and to establish a procedure for the periodic compilation and publication of policy statements. FDA recently committed to improving the procedures that govern the development and use of guidance documents. On March 6, 1996, FDA published a FEDERAL REGISTER notice soliciting comment on these issues.

Contracts for Expert Review/GMP Inspections. Section 403 authorizes FDA to contract with outside organizations or individuals in connection with the review of food additive and device applications . Section 405 permits FDA to accredit organizations to conduct inspections to evaluate manufacturers' compliance with gmp requirements. The concept of giving FDA authority to transfer the more "mundane" FDA functions to third parties is supportable.

Environmental Impact Review. Section 406 eliminates the requirement to prepare an environmental analysis unless FDA demonstrates a probability of substantial impact. As part of REGO, FDA will be proposing additional categorical exclusions to its National Environmental Policy Act procedures.

Pediatric Studies Marketing Exclusivity. Section 411 provides a 6 month marketing exclusivity for approved applications with pediatric studies submitted by an applicant. It is important to provide incentives for conducting pediatric studies. However, there are concerns about whether the provision is sufficiently tailored so that it applies to important new uses and as to whether the incentive is too generous in light of the fact that these trials often are very inexpensive.

Export of Drugs and Devices. Section 502(b) relaxes the export requirements that currently exist for unapproved new drugs and devices. As part of REGO, FDA agreed to seek legislation that would relax export requirements.

Pilot and Small Scale Manufacture. Section 603 provides that a new drug manufactured in a pilot or other small facility may be used to obtain approval prior to scaling up to a larger facility unless FDA demonstrates that a full scale production facility is necessary to assure safety and effectiveness. For most drugs, this currently is permitted.

Insulin and Antibiotics. Section 605 repeals requirements for lot and batch verification. FDA has done this under REGO.

Biological Products. Section 606 would regulate well characterized biologics as drugs. FDA is harmonizing the regulation of well characterized biologics and drugs.

Exemption of Class II Devices. Section 702, which gives FDA the authority to exempt class II devices from premarket notification requirements via a streamlined process, is beneficial.

Device Performance Standards. Section 708 requires FDA to recognize performance standards of certain standard setting organizations. The concept of greater regulatory use of consensus standards is supportable. However, there are a number of problems with the provision as drafted. For example, FDA should have the authority to decertify any standard setting organization and to decide which standards it will recognize. Companies should not be permitted to self-certify compliance with recognized standards. Even the EU requires third party certification.

Limitation of Residues. Section 803 would permit dose ranges to be used on animal drug labels. This provision, which would eliminate the requirement that FDA approve an optimal dose, the minimum dose at which there is a maximum effect, is supportable.

Veterinary Feed Directives. Section 805 creates a new class of animal drugs intended for use in animal feed. This new class is desirable because certain animal drugs administered through feed must be used under a veterinarian's supervision and thus, cannot be sold over the counter, but regulation under the traditional prescription systems is not practical.